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## PRESSING PROBLEMS OF CARDIO-VASCULAR PATHOLOGY

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## FOREWORD

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PRESSING PROBLEMS OF CARDIO-VASCULAR PATHOLOGY (12th Scientific Session of the Institute of Therapy of the Academy of Hedical Sciences USSR)

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The 12th Scientific Session of the Institute of Therapy of the ANN USSR /Academy of redical Sciences USSR was held 28-30 January 1961. The focus of attention at the session was on the most pressing problems of cardio-vascular pathology such as hypertensive illness, arteriosclerosis and coronary insufficiency. The session was attended by about 700 delegates who came from more than 90 cities of the Soviet Union. Taking part in the work of the session along with the therapeutists were representatives from the theoretical disciplines such as physiology, pathophysiology, morphology and biochemistry. Among the guests at the session was the leading Canadian scientist Hans Sellier who gave an interesting report devoted to the basic notions in the conception of the general adaptation syndrome.

Twenty-seven reports were heard at the session and they caused great interest among those attending, and elicited a broad discussion

in the debates. Thirty-five people took part in the debates.

The subject of the session encompassed various questions in the physiology and pathophysiology of the cardio-vascular system, and the biochemistry, pathogenesis, epidemiology and therapy for the diseases

in the organs of blood circulation.

At the first sitting reports were heard which dealt with the physiology and pathophysiology of the cardio-vascular system. They gave interesting materials and new information on the question of nervous regulation in blood pressure, heart activity and the functions of the coronary arteries. The reports convincingly upheld the concept of the absence of an antagonism between the sympathetic and parasympathetic nervous systems in their effect on blood pressure, the vascular system including the coronary arteries and the work of the heart.

The report of B. S. Kulayev entitled "The Influence of the Reflexogenic Zone of the Heart on the Cardio-Vascular System and Skeletal fusculature" contained data which had been obtained in acute experiments on cats. They studied the afferent impulsation which arises under chemical stimulation of the heart receptors. It was shown that with this there

occurs a reflector change of the general blood pressure while a weak stimulation caused only a small and momentary increase in the insensity of the afferent impulsation and pressor reactions. By increasing the strength of the stimulation the intensity rose proportionately, but not the qualitative characteristics of the afferent impulsation which led to the development of depressor reactions. Nevertheless it was shown that "pressor" or "depressor" afferent impulsation does not exist, but rather that the "pressor" or "depressor" character of the reaction is determined by the amount of simultaneously stimulating and homogeneous (in a functional sense) afferent fibers, and by the speed and duration of the impulsation in each of them. The author explained that the change in the level of general blood pressure arises under the influence of a change in heart activity and as a result of a change in the peripheral resistance of the vessels. However the tonus of the vessels in various parts of the body did not change in a similar fashion. The greatest tonic influence of impulsation from the heart was felt on the vessels of the small intestine and intestine, then to an insignificant degree on the vessels of the skin, head, heart, skeletal muscles, kidneys and spleen. From an analysis of the materials, the author came to the conclusion that the character of the vasomotor reaction (vascular-contracting or vascularexpanding) depends on the intensity of the homogeneous afferent impulsation along the vasomotor fibers of the sympathetic nervous system. The speaker further touched on the disturbance of the buffer-compensatory properties of the cardio-vascular reflexes which he observed under pathological conditions and particularly after a ligation of the coronary arteries when there was a distortion of these reflexes.

The results of the work enable one to consider that the heart as a reflerogenic zone plays a leading role in reflector self-regulation of blood circulation and the disruption of its receptive function can be the reason for the origin of pathological conditions or the exacerbation of earlier existing ones.

The next report of I. H. Rodionov, and V. P. Kulagine entitled "Certain Regular Patterns in Heuro-Humoral Regulation of Vascular Tonus" developed a number of concepts which were touched on by the first speaker. The idea presented from the experiemental research came down to the fact that the different types of action from the nervous system can cause two qualitatively different effects -- a contraction or expansion of the vessels. The authors do not consider it possible to speak of the existence of vascular-contracting or vascular-expanding nerve fibers. The individual fiber and the individual impulse do not possess the features which determine the character of the response. The latter arises only as a result of the tissue reaction to the stimulation. From this one may draw the conclusion that both the contraction and the expansion of the vessels is conditioned by the activity of one and the same nerve center where a change in the condition of this center under pathological conditions can have as a consequence a qualitative change in the reflector regulation of the vascular periphery.

Great interest was elicited from the delegates at the Session by the report of A. V. Trubetskoy entitled "Research on the Functions and Blood Supply of the Heart with the Aid of the Method of Artificial Blood Circulation." The author undertook an attempt at finding a new theoretical approach and a new methodological procedure for solving the question of nervous regulation in coronary blood flow. In the experiments research was carried out on a method of humoral isolation of the heart which was done on cats and dogs with the aid of two perfusion machines for artificial blood circulation. One of them supplied blood for the entire organism while the other only for the heart muscle. The nerve connections of the heart with the central nervous system were preserved in tact. Such a method enabled the author to investigate various aspects in the regulation of the cardio-vascular system and to study the action mechanism of drugs which are used for cardio-vascular diseases. The speaker showed the possibility of a method for the humoral isolation of the heart. In particular under the research on the heart as a reflexogenic zone of the vascular and respiratory system, data was obtained which characterized the heart as a buffer-compensatory reflexogenic zone. In view of this, the data presented affirm the material of B. S. Kulayev which was given in the first report. Experiments substantiated the existence of a coordinating relationship between the respiratory and cardiovascular centers. Finally, in the experiments, they studied the action of adrenalin, nitroglicerine, acetylcholine and pituitrin on coronary bloodflow and the myocardium. It was disclosed that adrenalin at the beginning of its action limits coronary blood flow and then increases it strongly and for a long period of time. In addition, adrenalin increases the contracile tonus of the myocardium (experiments on a fibrillating heart) and increases the myocardium's need for oxygen. Nitroglicerine in acting through the nerve apparatus expands the coronary vessels and increases the requirement of the myocardium for oxygen. Acetylcholine expands the coronary vessels and decreases oxygen requirements; pituitrine contracts the heart vessels and decreases the requirements of the myocardium for oxygen.

Hence the creation of a method for the humoral isolation of the heart provides an opportunity for an extensive study of the most important questions of the physiology, pathophysiology and pharmacology of

the heart and coronary blood flow.

The report of V. S. Sal'manovich "The Study of the Sequence of the Spread of Stimulation into the Heart Under Hyperkalemia" was a fine example of successfully using delicate electrophysiological analysis in evaluating the functions of the myocardium. In view of the absence of a possibility of studying with the aid of an electrocardiographical method the changes in the bioelectric properties of the heart under the conditions of hyperkalemia which is frequently found in clinical practice, the author jointly with Ye. K. Luk'yanov proposed an original modification of the vector method for investigating the sequence of the spread of stimulation in the myocardium. Under the conditions of an artificially induced state of hyperkalemia in cats, they determined the potassium content

in the blood plasma and on an exposed heart they recorded with the aid of electrodes a vectogram from various parts of the heart; at the same time an electrocardiogram was taken. It was discovered that in healthy animals the stimulation begins in the paraseptal area of the right ventricle and then the stimulation encompasses the paraseptal area of the left ventricle. Then the stimulation spreads into the crown of the right and left of the heart and finally to the lateral surface and to the base of both ventricles. Under hyperkalemia the sequence in the spread of stimulation in the heart is essentially changed. Thus, a small increase in the potassium level in the blood plasma is accompanied with a rapid stimulation of all areas of the myocardium. Under large concentrations of potassium one notes a retarding in the inception of stimulation in all areas of the myocardium. With this one observes the development of an intraventricle blockading action and the origin ectopic foci, extrasystole and finally there is a cardiac arrest in the diastole. All of these changes are reversible and are easily removed with the normalization of the potassium level in the plasma.

As for the electrocardiogram, the change in the QRS complex begins only with a significant increase in the potassium content in the plasma, when there is already a very marked disruption in the time of the stimulation of various parts of the myocardium. On the basis of his data, the author poses the question of the inadequancy of evaluating the condition of the myocardium in patients with hyperkalemia according to the analysis

of one electrocardiogram.

The report of V. L. Karpman, H. A. Abrikosova and G. A. Glezer was devoted to the hemodynamic mechanisms of increasing arterial pressure in hypertensive illness. In 107 patients at various stages of the illness they determined the minute volume and peripheral resistance. By applying a respective equation the authors gave an exact mathematical analysis of the results of the observations, and came to the conclusion that there exist various mechanisms for increasing arterial pressure which with varying frequency are encountered among patients with hypertensive illness. Thus, for example, in a part of the observations they noted a comparative increase in peripheral resistance which did not coincide with a proportional decrease in the minute volume. In other cases on the contrary they found a comparative increase in the minute volume without a corresponding decrease in the magnitude of peripheral resistance. The next group of reports dealt with certain biochemical aspects

in the study of arteriosclerosis and myocardial infarct.

The report of N. G. Kritsman and A. S. Alekseyeva was devoted to the question of the role of enzymes in the pathogenesis of arteriosclerosis. In their preceeding research, the authors had brought out under experimental arteriosclerosis the change in the activeness of a number of enzymes in the cardio-vascular system and the liver. The report gave the results of research on the activeness in the blood of the enzyme system from the cycle of tricarboxylic acid. The authors proceeded from the view that arteriosclerosis is accompanied by changes in the lipid, albumen and carbohydrate volume, but that the cycle of tricarboxylic acids is the chief means for oxidation and the deoxidation of intermediate products in the conversion of lipids, albumens and hydrocarbons.

The activeness of the investigated enzymes was determined spectrophotometrically. The results of the experiements show that under experimental arteriosclerosis the activeness of the enzyme system changes
essentially. At various stages of the experimental arteriosclerosis they
observed that in the serum there was a regular increase in the activeness of the dehydrase of lactic acid. The activeness of the aminoferous
enzymes which catalyze a reversible conversion of glutamic, pyrotataric
and oxalectic acids in these same animals is markedly decreased.

In analogous experiments they did not note the strict regularity in the change of activeness in the dehydrases of malic, succinic, citric, fumaric and other acids. Thus the materials from the work substantiate the notion of the significance of certain coenzymatic factors in the

disruption of enzyme activity in arteriosclerosis.

The data on the amino acid composition of the lipoproteins of blood serum under normal conditions and under artificial arteriosclerosis was given in the report of B. S. Sukhareva. For the research they used a method of electrophoretic separation of the lipoproteins on paper, and the method of controlled chromatography of amino acids with their subsequent quantitative determination with the aid of the SR-4 spectrophotometer. In the alpha- and beta-lipoproteins quantitatively they determined the 15-amino acids (cystine, lysine, histidine, arginine, aspartic acid, serine, glycine, glutamic acid, threonine, alanine, methionine+valine, phenylalanine, leucine+isoleucine).

The data which were obtained showed that the amino acid composition of the albumen part of the lipoproteins under arteriosclerosis qualitatively did not change. However they did note in this certain quantitative changes: a decrease in the serine and glycine content in the alpha-lipoproteins, and a lowering of the serine, glycine and agri-

nine content in the beta-lipoproteins.

The two following reports of L. G. Yefimova and A. A. Mekrasov were of great practical significance for the diagnostics of myocardial infarct.

The first report dealth with certain enzymes which catalyze the processes of reaminicizing amino acids. During acute myocardial infarct they did research on the free amino acid content in the blood serum such as alanine, glutamic and aspartic acid, agrinine, lysine and cystine. For these results they used the method of single-measure descending paper

chromatography.

It was discovered that in patients with acute myocardial infarct, beginning with the third day of the illness there is a significant increase in the glutamic acid, arginine and lysine content, and in the usual course of the illness the changes last 1-5 days and in severe cases from 15-17 days. In a control group of patients with chronic coronary insufficiency and also in patients after an attack, the glutamic acid, arginine and lysine do not exceed the normal limits.

The results of the work of  $\Lambda_{ullet}$  A. Mekrasov was an elucidation of the comparative diagnostic value in myocardial infarct of the following three enzymes in blood serum; aspartic, alanine transminase and aldolase.

The data obtained showed that the most sensitive and characteristic feature for the development of a focus for necrosis in the myocardium is an increase in the aspartic transaminase in the blood serum over the course of 4-5 days of the illness under a favorable course and over 10-15 days under severe conditions. The author found a small increase in aspartic transaminase in the first 12-2 days in patients with small focal changes of the myocardium which had no clear electrocardiographic indications. Along with the aspartic transaminase, in acute infarcts the author observed an increase in aldolase and a small change in alanine transaminase. in alanine transaminase.

The increase in alanine transaminase was most marked in patients with chronic liver disease. In a number of cases of severe lung diseases the activeness of aldolase grew. Thus it is possible to use simultaneous research on the three enzymes of blood serum in uncertain cases for differential diagnostics between a myocardial infarct and an affection

of the liver or lungs. At the end of the first session the Canadian scientist Hans Sellier gave a report devoted to the basic precepts in the conception of the general adaptation syndrome. The report brought out convincing facts and theoretical considerations based on these facts which explain the role of certain humoral agents (of a hypophysial-adrenal nature) in the origins of a number of diseases. In this the Canadian researcher especially stressed the great significance of the works of I. No. Sechenov, H. Ye. Vvedenskiy and I. P. Pavlov for a study of the problem of adaptation. In the opinion of Sellier, the humoral concepts which he advanced only supplement the neuro-reflector theory of the genesis of pathological conditions in the organism. The unity and interconnection of the nervous system with the humoral factors is the key for the study of the nature of pathological processes.

The second sitting of the session began with reports devoted to

the questions of the pathogenesis of cardio-vascular diseases.

I. K. Shkhvatsbaya gave a report "The Experience in Reproducing Disruptions of Coronary Blood Circulation in Rabbits by the Means of a Yeurogenic Action." The author proposed and used in the experiments the method of direct action on the central nervous system in the form of a dosed injection of air in the lateral ventricle of the brain in rabbits. As a result of such an action it was possible to trace the regular pathological changes in the electrocardiogram which attest to an acute ischemia of the myocardium. These changes were often preceeded by various disruptions in the rhythm and changes in the conducting system of the heart. In morphological research on all of the 20 rabbits which had air injected into the brain cavity, there was disclosed structural impairment of the myocardium with the formation of various (in extent) foci of necrosis and zones of granulized tissue. The changes were often dispersed subendocardially, sometimes transmurally.

Further research by the author which was directed at elucidating the role of the extracardial nerves in the development of the observed pathological changes showed that their origins is conditioned by a sharp activation of the sympathetic nervous system in response to the injection of air into the brain chamber.

The report of L. V. Kasatkina took up the significance of the local vascular action in the pathogenesis of experimental arteriosclerosis in rabbits. The author effected the permeability of the fascular walls with hyaluronidase. The data which were obtained attested to the strengthening of the artiosclerotic process under the influence of the hyaluronidase with the absence of the latter's action on the level of alimentary cholesteremia. In the opinion of the speaker, such an influence of the hyaluronidase on the development of experimental arteriosclerosis is conditioned by the increase in the permeability of the arterial wall which is caused by the depolarization of the mucopolysaccharides in the wall's basic substance.

The report of Ye. N. Gerasimov "On the Role of Certain Corticosteroids in Hypertensive Illness" gave interesting data which had been obtained from a determination of the amount of mineral corticoid of aldosteron in the urine of patients with hypertensive illness. The research showed that the precipitation of the aldosteron at the outset of the illness is little different from the amounts obtained from healthy persons, while during the further progressive stages of the illness and in the more severe forms it increases sharply. There was observed a marked decrease in the precipitation of the aldosteron from the urine under the influence of the treatment with hexamethonium under the conditions of its clear hypotensive action. It is worth noting the fact that there was discovered in the patients! urine along with the aldosteron substances which have the chemical properties of corticosteroids. Under biological testing on adrenalectomized rate it was shown that this substance decreases the precipitation of potassium, ic., it is an antagonist to the aldosteron.

The report of V. V. Hen shikov again touched on the question of the role of the adrenals in the pathogenesis of hypertensive illness. For an evaluation of the function of the sympathoadrenal system, the author investigated the determination of free catechol amines—adrenalin and noradrenalin—in the urine. Quantitative determination of the catechol amines in the urine was carried out with the aid of a modified fluorimetric method.

It was discovered that in healthy patients, the precipitation of the catechol amines from the urine increases under the influence of stimulants of the sympathoadrenal system (emotions, physical tension, smoking, pain) and decreases under the action of factors which lower the activity of this system (sleep, physical rest, ganglionic blocking agents, adrenal ectory).

Further the author showed that hypertensive illnes is accompanied by a normal or even reduced precipitation of catechol amines particular to the 2nd and 3rd stages of the illness. However, in the opinion of the speaker this did not mean that the catechol amines play no role in the pathogenesis of hypertensive illness. It is essential to consider that under pathological conditions the exhlange of catechol amines may mask their increased production in the organism, and as a result give a normal or lowered catecholaminuria. Thus for a decisive solution to the question, we must have a complex study of the catechol amines in patients with hypertensive illness beginning with the production of adrenalin and noradrenalin and ending with their precipitation from the urine.

The report of A. A. Stupmitskiy (Kuybyshev) shed further light on certain insufficiently clear questions in the pathogenesis of cardiac as thma. The author presented the results of research on the function of the heart and the condition of lesser /pulmonary/ circulation in patients with cardiac asthma, and gave a comparison of them with the same indices for patients with bronchial asthma. Further support was given to the current opinion on the fact that in bronchial asthma the basic clinical manifestations depend upon bronchiospasm while in cardiac asthma they are determined by hemodynamic disruptions and above all in the lesser circulation. Without denying here the significance of the weakening in the function of the left ventricle, the speak stated that in an attack of cardiac asthma there occurs a lowering in the function of not only the left but as well the right ventricle. Under these conditions one observes an increase in the blood pressure in the sulmonary artery and a retardation in the speed of blood flow in the lesser circulation with a congestion in it, and a lowering of the general blood pressure. The indicated symptoms in the author's opinion are the result of a spasm of the pulmonary arteries. Hence the crisis of the vessels of the lesser circulation is viewed as one of the leading links in the development of attacks of cardiac asthma. The author considered the good curative effect from Eufilline, hexamethonium, reserpine and morphium.

In the section of "Clinical Epidemiology" 5 reports were heard, the first of which took up the distribution of myocardial infarct among the population of various districts of the USSR in relation to the character of the diet and the cholesterol level in the blood. I. S. Clazunov determined in four cities (Tallin, Stalinabad, Ryazan' and Arkhangel'sk) the cholesterol level in the blood of white collar workers (a total of 2100 persons), and studied the statistical data on the fat requirements of the population in these cities and the mortality rate from myocardial infarct. The highest average figures for cholesteremia and the highest mortality from myocardial infarct were found in Tallin where animal fats predominate in the food of the population.

In Stalinabad where vegetable fats predominate in the food, the mortality from myocardial infarct was the lowest while cholesteremia was less than in Tallin.

Thus it has been established that there is a definite correlation between the amount and type of fats in the food, the degree of cholesteremia and the mortality from myocardial infarct.

of arteriosclerosis in 500 young and practically healthy persons from

20 to 40 years of age. In 13.4, of the cases there was found hypercholesteremia which often coincides with the signs of arteriosclerosis of the aorta and hypertensive reaction. It was shown that family inheritance of a predisposition for arteriosclerosis in persons with hypercholesteremia is found significantly more often than in persons with a normal level of cholesterol in the blood.

The reports of K. H. Zayslova and H. K. Belyayeva raised the question of the coincidence of hypertensive illness and arteriosclerosis.

An analysis of 3300 histories of the illness showed that the frequency of coincidence of arteriosclerosis and hypertensive illness is very great (37.4 from the total of all cases of hypertensive illness and arteriosclerosis). The consequence of one or the other process can be different. There is a particularly close link of these diseases in the beginning and terminal phases of the illness. Further indication of this is the rather frequent coincidence of similar indications of family anamnesia and the presence of arteriosclerosis in almost all of the cases of hypertensive illness of the 3rd stage. The character of the changes in the electrocardiogram and the general course of the shifts of lipid exchange supplement the similarity of the illness processes. The data given support the hypothesis of A. L. Iwasnikov on the possible pathogenetic commonness of arteriosclerosis and hypertensive illness.

The facts which support the justification of the hypothesis given above also figures in the report of L. P. Bondar. The author did research on the relationship of alpha- and beta-lipoproteins in blood serum for 282 patients with arteriosclerosis of the coronary vessels without hypertensity, with hypertensive illness with the clinical manifestations of arteriosclerosis and in the coincidence of these diseases. In the pathological states under investigation and in particular with the presence of arteriosclerosis, there was observed a common trend in the shifts in the relationship of the lipoprotein fractions.

The second sitting concluded with a report by Yu. I. Pronin on "The Question of the Link Between Adiposity and Arteriosclerosis." In a comparison of the group of patients with arteriosclerosis with adiposity, they showed a definite difference in the individual clinical and biochemical indices. The author came to the conclusion that with adiposity, arteriosclerosis develops earlier, has a more severe course and is accompanied by a deeper disruption of the lipid exhange.

The third and last sitting of the session was devoted to the

therapy of cardio-vascular diseases.

The report of Te. I. Chazov and G. V. Andreyenko gave new data on the curative application of fibrinolysin for experimental thrombosis; this substance was obtained in the Laboratory of Biochemistry and Physiology for Blood Coagulation of the Roscow State University. The study of the action of fibrinolysin was conducted on various models of thrombosis on the coronary and peripheral vessels in healthy animals and under experimental arteriosclerosis. The substance was given intravenously and brought about a sharp increase in the fibrinolytic activity of the blood. The application of fibrinolysin led to the lysis of fresh thrombi including

those in the coronary vessels and to a return in a number of cases to normal blood with the absence of any side effects. The authors posed the question of the possiblity of transferring the study of the action of fibrinolysin into clinical conditions.

H. A. Ratner, G. L. Spivak, G. A. Glezer and U. B. Sharapov spoke on the diuretic and hypotensive action of the new sulfanilamide compound, hypothiaside. It was established that hypothiaside possesses a good hypotensive action in patients with hypertensive illness at various stages, and even under persistent and resistent hypertensiveness. The hypotensive action of the preparation is always accompanied by a diuretic effect particularly in patients with hypertensive illness with an insufficiency in blood circulation and edemae. A marked diuretic effect was obtained in patients with edemae of a non-cardiac origin. It was explained that the diuretic action of hypothiaside is always linked with the significant fall in sodium with a simultaneous increase in the potassium precipitated from the urine. The renal mechanism of its diuretic action is caused chiefly by a decreased reabsorbtion of the sodium and water in the ducts. As for the hypotensive effect of the preparation in the opinion of the authors it is caused by the decrease in the volume of plasma and minute volume in the blood and also by the ability of the hypothiaside to decrease the sodium gradient in the muscle tissue of the peripheral vessels and thus lower peripheral resistance.

U. B. Sharapov observed an equally effective diuretic action in patients with circulatory insufficiency under the conditions of applying Novurite and Diacarb (Diamox). The diuretic action meachanism of Novurite depended on lowering the reabsorbtion of sodium in the ducts and a simultaneous decrease in the reabsorbtion of water. The diuretic effect of Diacarb was also caused by a lowering of the reabsorbtion of sodium ions which in its turn was linked with a depression in the activeness of carbon anhydrase. In the process of the increase in sodium diuresia under the influence of the Diacarb, there was also noticed an in-

crease in filtration.

The authors of both reports strongly recommended a wider application of hypothiaside, Hovurite, and Diacarb in the clinical treatment of

cardio-vascular diseases.

L. H. Ignatov spoke on the mechanism of the curative effect of vitamin Bl2 during arteriosclerosis. In the work, a study was made on the changes in the choline, methionine, cholesterol and phospholipid content in patients with arteriosclerosis with vitamin B12 treatments. On the basis of the data obtained, the author came to the conclusion that the change in the cholesterol level in the blood serum of patients with arteriosclerosis under these conditions is caused by the strengthening of the transmethylation reaction which leads to a synthesis of strong lipotropic agents -- choline and phospholipids.

. K. Haslova gave her observations on the dynamics of the basal metabolism during vitamin C and B12 treatment for patients with arteriosclerosis. Here in all cases along with the significant lowering of the basal metabolism, the author observed an increase in its indices against initial figures which coincides with a lowering of the cholesterol level

in the blocd.

Outside of the announced program additional reports were given by A. M. Korolev (Kirov) "Sensory Chronaria in Patients with Hypertensive Illness" and N. S. Kel'ginbayev (From the Institute of Kray Medicine of the Uzbek Academy of Sciences) "The Manufacture and Pharmacoligical Action of the Domestic Strophantine-K."

The numerous delegates of the session who spoke in the discussion gave a high evaluation to the reports heard in noting their novelty and

foward-looking character.

In the closing speech the Active Member of the AMM USSR, Professor A. L. Myasnikov summed up the results of the session's work and laid down further prospects for research in the area of cardio-vascular pathology.